EXPERT REVIEWS

# Integrative computed tomographic imaging of coronary artery disease

*Expert Rev. Cardiovasc. Ther.* 9(1), 27–43 (2011)

Markus Weininger†1, Matthias Renker1, Garret W Rowe1, Joseph A Abro1, Philip Costello1 and U Joseph Schoepf1,2

[1]*Medical University of South Carolina, Department of Radiology and Radiological Science, Ashley River Tower, 25 Courtenay Drive, Charleston, SC 29401, USA*
[2]*Department of Medicine, Division of Cardiology, Medical University of South Carolina, Charleston, SC, USA*
†*Author for correspondence:*
*Tel.: +1 843 076 4215*
*Fax: +1 843 876 3157*
*weininge@musc.edu*

Rapid technological evolution in multislice computed tomography (CT) over the last decade with improved spatial and temporal resolution has enabled cardiac CT to become a viable and effective alternative in the diagnosis of coronary artery disease. Within recent years CT coronary angiography has demonstrated high sensitivity and specificity, and in particular a very high negative-predictive value, making it a valuable imaging modality for ruling out suspected coronary artery disease. In addition, CT angiography demonstrates accuracy in the detection and characterization of coronary plaques, and it has been reported to play an important role in predicting disease progression and cardiac events. The goal of this article is to provide an overview on the role and current clinical applications of cardiac CT in the evaluation of coronary artery disease. Emerging areas of cardiac CT, including dual-energy CT and CT myocardial perfusion are also discussed, as well as the limitations and future directions of cardiac CT.

**Keywords:** cardiac computed tomography • coronary artery disease • dual-energy computed tomography • dual-source computed tomography • myocardial perfusion computed tomography

Coronary artery disease (CAD) represents the most relevant cause of death and morbidity in the adult population of developed and developing countries [1,2]. During the last decades, strong research and financial effort has been made to identify more selective biomarkers and refine imaging technologies to better assess the cardiovascular risk in both primary and secondary prevention [3].

Rapid technological advances have made computed tomography (CT) a widely embraced modality in the non-invasive evaluation of CAD [4]. The capabilities of multidetector row CT (MDCT) to identify and rule out significant coronary artery stenosis have been consistently confirmed and clinically embraced as a core application of cardiac CT [5–13]. For comprehensive imaging of the heart, CT has been evaluated for the assessment of the myocardium, myocardial perfusion and viability, cardiac function, wall motion, as well as cardiac valves [14–20]. Nevertheless, the diagnostic value of cardiac CT beyond strict morphological evaluation of coronary stenosis remains uncertain. It proved to be surprisingly difficult to predict the hemodynamic relevance of stenosis and further stratify risk by detailed plaque characterization strictly based on anatomical information acquired during CT coronary angiography [21,22].

However, most recent advances in CT technology, including larger detector coverage and the availability of two generations of dual-source CT (DSCT) systems combined with substantial research efforts focused on plaque characterization and identification of positive remodeling suggest the feasibility of CT as a standalone modality allowing an integrative assessment of all aspects of coronary heart disease [23–26].

The purpose of this article is to review current and future applications of cardiac CT in the evaluation of CAD.

## Technical evolution

In 1984, electron-beam CT was introduced as the first system capable of ECG-synchronized CT imaging of the cardiac anatomy [27]. The rapid rise of cardiac CT from a research application to a clinically appreciated modality was mainly driven by the introduction of MDCT. Since 1998, four-slice CT systems with higher volume coverage speed and improved temporal resolution of 250 ms have been clinically used for cardiac examinations at low to moderate heart rates, enabling quantification of coronary artery calcification and initial evaluation of coronary artery stenosis, cardiac function and the analysis of atherosclerotic plaque [28–33]. With each subsequent scanner

 10.1586/ERC.10.166  ISSN 1477-9072 

generation and improvement in temporal resolution, the proportion of successfully examined patients with non-invasive coronary CT angiography gradually increased [34]. The introduction of 64-slice CT systems in 2004 further increased temporal resolution up to approximately 165 ms, enabling detailed image acquisition of the heart with a 5–10 s scan time [35,36]. However, temporal resolution in patients with high heart rates and irregular heart rhythm was still limited, making pharmacological modulation for heart rates above 60–70 beats per minute (bpm) essential [37,38].

With the introduction of DSCT in 2006, a new scanner concept was presented consisting of two x-ray tubes and two detectors mounted perpendicularly in the same gantry [39]. This configuration allows full image reconstruction during quarter-rotation scanning as opposed to half-rotation scanning with conventional single-source multidetector CT systems, improving the temporal resolution to approximately 83 ms, reflecting one-quarter of the gantry rotation time [39,40]. With the recent introduction of second-generation DSCT, a 'high-pitch single-heartbeat acquisition' became feasible. In early reports, the ability of DSCT to perform ECG-triggered spiral data acquisition using very high pitch values (≥3.0) has been described. The application of high pitch values allows for an image acquisition of the entire volumetric data set of the heart within one cardiac cycle. As pitch is inversely related to radiation exposure, this scan mode is associated with approximately one-tenth of the exposure of a retrospectively ECG-triggered spiral scan and half to one-third of the dose of a prospectively ECG-triggered scan [41,42].

Motivated by the concept to completely cover the scanning volume within a single heart beat, 256- and 320-row single-source systems, as well as 128-row dual-source CT scanners, have been introduced recently [43,44]. The availability of detector arrays that are wide enough to cover the entire cardiac anatomy also enables new approaches in the assessment of cardiac function, including the acquisition of dynamic, time-resolved data on myocardial perfusion and the myocardial blood supply. These advancements may also reduce patient radiation and susceptibility to arrhythmia [43–45].

Furthermore, dual-energy acquisition techniques for the evaluation of myocardial blood supply based on static, non-time-resolved CT coronary angiograms using DSCT are being investigated [46,47]. Operated in dual-energy mode, the two-tube configuration of DSCT enables the simultaneous acquisition of high and low x-ray energy spectra with a single CT scan, permitting analysis of myocardial blood supply by determining the iodine (and thus blood) volume of the myocardium [46–48].

In addition, alternative image reconstruction approaches are being introduced that hold promise to realize substantial artifact and noise reduction, while at the same time increasing image sharpness, thus consequently increasing the accuracy of stenosis detection with coronary CT angiography, enabling a more precise delineation of calcified plaques and enhancing diagnostic capabilities to detect restenosis in coronary artery stents. The term 'iterative reconstruction' is used for a variety of approaches that either rely on ray-tracing in the image to calculate synthetic projections that are then compared with the originally measured projections to derive correction terms, or translate the iteration process into the image domain by performing an iterative chain of locally adapted nonlinear image processing steps. Although increased spatial resolution is directly correlated with increased image noise in standard filtered backprojection reconstructions as they are used in CT scanners today, iterative reconstruction approaches to a certain extent allow the decoupling of spatial resolution and image noise. In an iterative reconstruction, a correction loop is introduced into the image reconstruction process. Iterative corrections are performed with further image noise reduction without degrading image sharpness, and involve a comparison of an initially reconstructed master image with a corrected image. Besides an increase in diagnostic accuracy, the decrease in image noise provided by iterative reconstruction allows for a significant reduction of radiation dose in routine clinical use while maintaining similar signal-to-noise ratios as with standard radiation dose acquisition protocols [49,50].

## Coronary calcium scoring

Coronary calcium scoring using CT has been validated as a useful imaging tool for risk stratification and reclassification of the risk of CAD [51]. Atherosclerotic lesions of the coronary arteries often contain calcified components that used to be accurately measured by electron beam CT, but this method has been replaced by MDCT applying the Agatston scoring methodology [52,53]. Recent guidelines from the American Heart Association reviewed scientific data for cardiac multislice CT imaging of CAD and atherosclerosis in symptomatic and asymptomatic patients, and approved screening using calcium scoring as a methodology to reclassify risk in patients with an intermediate risk based on traditional scores such as the Framingham and Procam algorithms [54]. Further effort has been undertaken to correlate atherosclerosis to different pathological processes. One example is the Rule Out Myocardial Infarction Using Computer-Assisted Tomography (ROMICAT) trial, which sought to determine whether aortic valve calcification is associated with the presence and extent of the overall plaque burden, as well as with plaque composition. As a result it was suggested to consider aggressive medical therapy if aortic valve calcification was present [55].

Computed tomography calcium scoring is usually performed as a screening method in a low radiation dose scanning technique to detect and calculate the density, volume or mass of calcified plaques. The total coronary calcium burden is used for prognosis and risk stratification in CAD. The underlying rationale is the concept that coronary artery calcification is part of the atherosclerotic degeneration of the arterial wall, and coronary atherosclerosis is the only disease associated with calcium in the coronary arteries [56]. Thus, measurement of the amount of calcium allows for an accurate estimation of the amount of coronary atherosclerosis and, therefore, the risk of CAD. The total calcium score is calculated by adding up the volume of calcium in all coronary arteries by a weighting factor, dependent on the density of each calcified plaque. Calcium scoring is regarded as a good and independent predictor of cardiac events and adds incremental prognostic value to other risk factors [57,58]. Increasing degrees of coronary calcium scores predict adverse cardiovascular events and all-cause mortality [57,59–61].

Patients with a normal or zero calcium score fall into the lowest risk category, and are thus associated with a low risk of cardiac events, or are considered to be clinically absent of any major atherosclerosis [57,60,62]. The predictive value of this methodology has been further supported recently. In their study, Min *et al.* aimed to identify the incidence and predictors of conversion for a normal to abnormal coronary artery calcium score over a period of 5 years [59]. They concluded that the rate of conversion to an abnormal calcium score was nonlinear and occurred at a low frequency before 4 years of follow-up, suggesting that repeat calcium scoring examinations should not be performed for a minimum of 4 years in individuals with a normal calcium score of zero [59]. However, even though a negative calcium score is associated with a low risk for developing cardiovascular events in the following 2–5 years, it may not exclude luminal obstructive disease, especially in patients who are young and present with acute coronary syndrome [63–65]. Rubinshtein *et al.* concluded that 7% of patients with acute or long-term chest pain who had zero calcium score at CT were found to have significant CAD [66]. According to the literature the cumulative incidence of a zero or low calcium score is associated with a risk of 0.1 and 0.7% of cardiac events with a follow-up period of 3–5 years [52]. In addition, thickness of reconstructed slices is important as 3.0-mm or thicker slice reconstructions result in missing calcified lesions compared with 0.5-mm slice reconstructions [58,67].

Despite the recognized limitations of this test, coronary calcium scoring is currently seeing renewed interest as an aid for further cardiovascular risk stratification and risk factor management in both asymptomatic and symptomatic populations [51]. The technology is seen as an opportunity to non-invasively assess the progression of CAD and monitor the clinical efficacy of medical therapies by tracking the changing calcium score. As clinical decision making regarding the need for medical intervention can often be uncertain in asymptomatic individuals with one or more conventional risk factors for coronary disease, a technology such as coronary calcium scoring might become integral [68]. The importance of calcium scoring for clinical decision making was recently acknowledged by Polonsky *et al.* [69]. Their study demonstrated that adding calcium scoring to traditional risk factors results in a significant improvement in the classification of risk for the prediction of cardiovascular events in an asymptomatic population sample. They concluded that the use of calcium scoring plus traditional risk factors substantially enhances the ability to classify a multiethnic cohort of asymptomatic persons without known cardiovascular disease into clinically accepted categories of risk of future cardiovascular events.

To date, asymptomatic individuals with intermediate cardiovascular risk are seen as candidates for CT coronary calcium screening to allow improved risk stratification and to determine the level of aggressiveness of risk factor modification. In high-risk individuals the role of coronary calcium screening is still debated [54]. Further guidance can be expected with the upcoming update of the American College of Cardiology/American Heart Association recommendations. Nevertheless, additional integrating evidence regarding all available techniques is needed to determine the most practical and effective system for assessing cardiac risk to optimally target and follow the effect of preventive measures.

## CT coronary angiography

Over the last decade, there has been increasing interest in the imaging and diagnosis of CAD using multislice CT owing to its non-invasive nature and fast scanning technique with extended z-axis coverage. Early studies using four-slice and 16-slice CT showed moderate diagnostic accuracy with pooled sensitivities and specificities of 78 and 93%, and 82 and 95%, respectively [28,35,68,70,71].

With the introduction of 64-slice CT and substantial improvements in spatial and temporal resolution, pooled estimates of assessable segments for CT coronary angiography increased to 97%, assessable segments were found to improve with the increase of CT detectors and significant difference was reached comparing 64-slice with four- and 16-slice scanners [71]. In the Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography (ACCURACY) prospective multicenter study of patients with chest pain without known CAD and intermediate disease prevalence, 64-slice CT angiography had a patient-based sensitivity of 94% and specificity of 83% in detecting coronary stenosis of 70% or more [72]. In the Coronary Artery Evaluation Using 64-Row Multidetector Computed Tomography Angiography (CORE-64) prospective multicenter study of patients with suspected symptomatic CAD, 64-slice CT angiography had a patient-based sensitivity of 85% and specificity of 90% for detecting coronary stenosis of 50% or higher [73]. However, in both studies patients with heavy coronary artery calcifications were excluded. Other representative studies evaluating the performance of 64-row CT and DSCT for detecting hemodynamically significant coronary artery stenosis report sensitivities between 86 and 99%, specificities between 92 and 98%, positive-predictive values between 47 and 91%, and most importantly negative-predictive values between 92 and 100%, allowing a reliable non-invasive exclusion of significant coronary artery stenosis using CT [11,21,38,74–77]. The predictive value of this methodology has been further supported recently. In their study, Min *et al.* aimed to investigate the prognostic value of CT coronary angiography for the prediction of major adverse cardiovascular events [78]. They concluded that the CT coronary angiography presentation of plaque severity and composition successfully identifies patients at risk for major adverse cardiovascular events and a negative CT scan portends an extremely low risk for incidence of such events. Table 1 provides a further overview of recent literature. Nevertheless, despite the rapid advances in scanner technology and image postprocessing, at times motion artifacts from high or irregular heart rates, excessive image noise in obese patients, and heavy vascular calcifications, especially with calcium scores above 400, result in limited diagnostic accuracy [56,79–81]. Further improvements in scanner technology suggest improvements in image robustness, especially in high and arrhythmic heart rates, the ability to evaluate heavily calcified vessels, and reduced blooming artifacts from heavy calcification and metallic stents using dual-energy [82–84].

Currently, however, besides heavy calcifications of coronary arteries motion artifacts remain the most important challenge for coronary CT angiography even with the latest generation of scanners making further evaluation in symptomatic yet inconclusive

**Table 1. Accuracy of 16-slice, 64-slice, 256-slice, 320-slice and dual-source computed tomography for the detection of coronary artery stenosis in comparison with invasive cardiac catheterization.**

| Author | Patients (n) | Sensitivity (%) | Specificity (%) | NPV (%) | PPV (%) | Ref. |
|---|---|---|---|---|---|---|
| *16-slice CT* | | | | | | |
| Kuettner *et al.* | 124 | 85 | 98 | 96 | 87 | [191] |
| Mollet *et al.* | 51 | 95 | 98 | 99 | 79 | [192] |
| Hoffmann *et al.* | 103 | 95 | 98 | 99 | 87 | [193] |
| Achenbach *et al.* | 50 | 94 | 96 | 99 | 69 | [194] |
| *64-slice CT* | | | | | | |
| Leschka *et al.* | 53 | 94 | 97 | 99 | 87 | [76] |
| Raff *et al.* | 70 | 86 | 95 | 98 | 66 | [80] |
| Leber *et al.* | 59 | 88 | 97 | 99 | | [132] |
| Nikolaou *et al.* | 72 | 86 | 95 | 97 | 72 | [195] |
| *256-slice CT* | | | | | | |
| Korosoglou *et al.* | 27 | 86 | 95 | 90 | | [153] |
| Chao *et al.* | 104 | 98.8 | 50 | 92.4 | 87.5 | [196] |
| *320-slice CT* | | | | | | |
| Dewey *et al.* | 30 | 100 | 94 | | | [197] |
| de Graaf *et al.* | 64 | 94 | 95 | 88 | 98 | [198] |
| *DSCT* | | | | | | |
| Leber *et al.* | 88 | 94 | 99 | 81 | 99 | [11] |
| Johnson *et al.* | 35 | 88 | 98 | 78 | 99 | [199] |
| Ropers *et al.* | 100 | 92 | 97 | 68 | 99 | [77] |
| Brodoefel *et al.* | 100 | 91 | 92 | 75 | 97 | [200] |

CT: Computed tomography; DSCT: Dual-source computed tomography; NPV: Negative-predictive value; PPV: Positive-predictive value.

patients necessary. In these patients additional non-invasive physiologic testing including nuclear myocardial perfusion imaging is recommended to identify intermediate but hemodynamically relevant stenosis [85].

In order to facilitate image interpretation and ensure diagnostic accuracy of stenosis identification, automated computer-aided detection solutions have recently been introduced (Figure 1). A recent study investigating the performance of a computer-aided detection algorithm for automated detection of significant stenosis at CT coronary angiography reported 100% sensitivity, 65% specificity, 76% accuracy, 100% negative-predictive value and 58% positive-predictive value compared with invasive cardiac catheterization [86].

To further guide referring physicians and radiologists in the use of this examination, the issuance of guidelines and appropriateness criteria by the professional societies has helped to define the indications for coronary CT angiography. There is consensus that coronary CT angiography is appropriate in symptomatic individuals, especially if symptoms, sex and age suggest a low-to-intermediate probability of significant coronary artery stenosis. There is also consensus that coronary CT angiography to date has no role for general screening for coronary atherosclerosis in asymptomatic individuals with low and intermediate cardiac risk (class III, level of evidence C), because the current levels of radiation are incompatible with the prerequisites of a successful screening test and data on the cost–effectiveness of this indication are lacking [54,87–93]. Whether CT coronary angiography has incremental value for risk stratification, risk modification and therapeutic monitoring in asymptomatic high-risk individuals is a topic of ongoing research [94].

## CT angiography of coronary artery bypass grafts

Invasive coronary angiography has been seen as the diagnostic standard for evaluating the status of both arterial and venous coronary artery bypass graft (CABG) vessels. However, CT has emerged as a promising non-invasive technique to visualize the coronary artery lumen and patency of the venous and arterial conduits. The anatomical features of arterial and vein grafts render these vessels specifically suitable for study with CT [95,96]. Because of their large size, relative immobility and lack of calcification, grafts appear ideally suited for evaluation compared with native coronary arteries [97]. While this applies mostly to venous grafts, arterial grafts (e.g., internal mammarian arteries) can be more challenging to evaluate due to their smaller vessel diameter and more frequent artifacts caused by metallic clips. Onuma *et al.* described limited evaluability of arterial grafts (90%) compared with venous grafts (99%) [98]. Recent studies comparing 16- and 64-slice CT with conventional coronary angiography describe sensitivities, specificities, positive and negative-predictive values up to 100, 95, 85 and 100%, respectively [98–100]. However, with sensitivities and specificities to detect significant stenoses as low as 83.3 and 80.2%, and up to 16% of distal run-offs nonassessable, evaluating the distal anastomosis and run-off arteries still remains challenging and might limit further clinical implementation [98,99,101]. Even though current data suggest attractive diagnostic potential in patients before or after cardiac surgery, the exact role of technological advances including DSCT in the exact evaluation of distal run-off vessels and anastomoses remains unclear and warrants further studies [102].

## Coronary artery stents

Percutaneous coronary intervention and stent placement is a preferred method for minimally invasive coronary reperfusion. However, even with the advent of drug-eluting stents that are engineered to reduce the cellular proliferation that results in

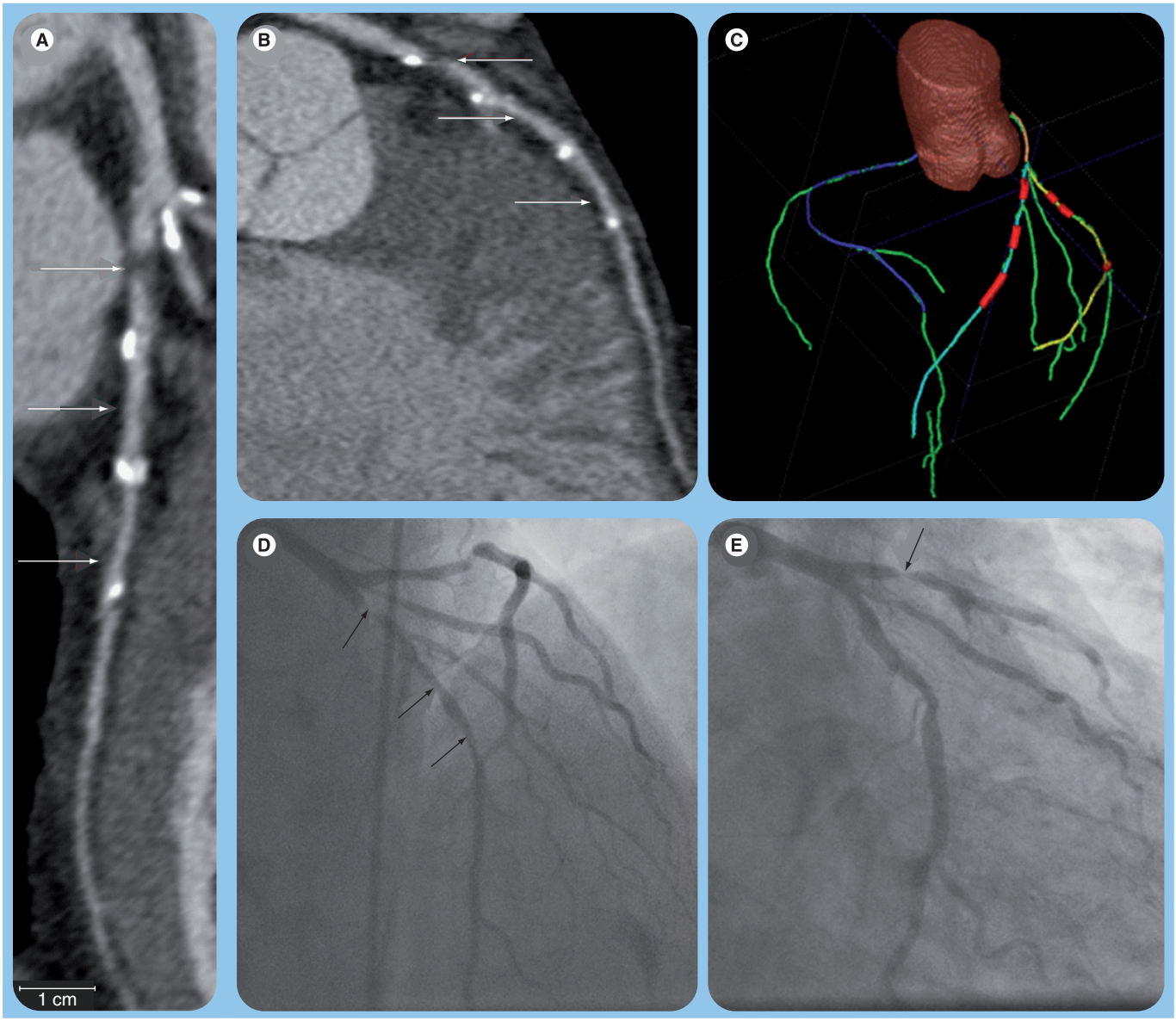


**Figure 1. A 52-year-old man with a history of hyperlipidemia. (A & B)** Curved multiplanar reformation of the left anterior descending artery and left circumflex artery shows several calcified and noncalcified plaques and stenoses (arrows). **(C)** Corresponding 3D segmentation by computer-aided detection algorithm, resulting in correct automated placement of detection markers. **(D & E)** Revealed stenoses were confirmed by invasive coronary catheterization.

neointimal hyperplasia, restenosis remains a common clinical problem, making early identification of crucial interest to prevent myocardial ischemia and improve prognosis [103].

Non-invasive assessment of coronary artery stent patency and detection of in-stent restenosis have been thoroughly investigated since the introduction of cardiac MDCT [104,105]. In clinical practice, stent patency is often determined by the visualization of contrast agent distal to the stent. However, patency can also be mimicked by collateral flow or retrograde filling. Conversely, the absence of contrast agent distal to the stent indicates severe in-stent restenosis [105]. The biggest challenge for MDCT technology is to overcome beam-hardening artifacts due to the stent's metallic composition and partial volume artifacts. With earlier scanner generations lumen assessment was often not possible due to artifacts and sensitivities remained low [106,107]. Stent assessment using 64-slice MDCT has provided further improvements; however, stent size, type and metallic composition still greatly influence diagnostic visualization [108].

A meta-analysis by Hamon *et al.* reviewed the role of MDCT in 15 studies including 807 patients and 1175 stents [109]. The results demonstrated a pooled sensitivity of 85% and a specificity of 91% for 64-slice CT. However, in these 15 studies 13% of stents were excluded from evaluation, which potentially overestimates the performance of MDCT, leading the authors to conclude that the clinical use of MDCT as an alternative to invasive catheterization for in-stent restenosis detection remains limited.

To date, there are only a few studies investigating the role of advanced scanner generations for the evaluation of stent patency. In their study Pugliese *et al.* showed a sensitivity, specificity, positive-predictive value and negative-predictive value of DSCT of 94, 92, 77 and 98%, respectively [110]. However, performance of DSCT is hampered by frequent false-positive findings in smaller stents (≤2.75 mm). Furthermore, Oncel *et al.* demonstrated sensitivity, specificity and positive and negative-predictive values of DSCT in the detection of in-stent restenosis or occlusion of 100, 94, 89 and 100%, respectively [111]. In their population only two out of 48 stents (4.2%) were misclassified as stenotic and later proven patent at conventional catheterization. Initial results with 320-slice CT show that CT angiography allows accurate noninvasive assessment of significant in-stent restenosis with sensitivity, specificity, positive and negative-predictive values of 100, 81, 58 and 100%, respectively, on a patient basis [9]. Besides quite promising results using newest scanner generations, the diagnostic performance of CT is mainly influenced by stent type, stent diameter and thickness of stents struts [112]. Based on these results, invasive catheter angiography remains the gold standard for the assessment of coronary in-stent restenosis [9,112]. Further studies performed with newer scanner generations should focus on improving imaging techniques to reduce artifacts resulting from the implanted stents.

## New & emerging applications

### *Cardiac function*

Left ventricular volumes and function are predictive markers of a variety of cardiovascular diseases, and left ventricular hypertrophy is an important prognostic marker in patients with or without CAD. In addition, patients with both CAD and depressed left ventricular function are at high risk for sudden death [113–116]. While transthoracic and transesophageal echocardiography are applied routinely and radionucleide ventriculography has been used, MRI has evolved into the preferred technique for the exact determination of cardiac function parameters [117–119]. However, with advances in CT scanner technology and the existence of isotropic voxels, image reconstruction can be performed in any desired plane [120]. Despite early reports about the underestimation of left ventricular ejection fraction, visual evaluation of wall motion abnormalities detected at cardiac CT showed good agreement with echocardiography and MRI, and further improved with current scanner generations [120–126].

Results obtained with modern CT scanner generations starting with 64-slice CT approach the accuracy of cardiac MRI, with a slight overestimation of end-systolic volume compared with MRI, resulting in a systematic underestimation of left ventricular ejection fraction that ranges from 1 to 7% [117,119,120,123,127,128].

Nevertheless, each time retrospectively ECG-gated cardiac CT is performed, data inherently contain image information of the complete cardiac cycle, which can be used to evaluate ventricular wall motion and global functional parameters for additional diagnostic benefit. With the introduction of modern postprocessing software, intuitive analysis of cine images and immediate quantification of functional parameters can be achieved, making the assessment of myocardial and valvular function an integrative part of the image interpretation for a comprehensive cardiac analysis [118,120,129].

### *Coronary atherosclerotic plaque imaging*

Since it has been shown that contrast-enhanced CT coronary angiography can sensitively detect coronary atherosclerotic plaques and differentiate between calcified and noncalcified atherosclerotic plaque components, there has been intense interest in the evaluation of coronary CT angiography as a tool for risk stratification and for monitoring risk factors [130–132]. The underlying rationale is a growing understanding of the relationship between plaque composition and different clinical manifestations of CAD. Symptoms of chronic stable angina correlate well with stenotic, mainly fibrocalcified lesions, whereas acute coronary syndrome and sudden cardiac death are more likely to be associated with a rupture of previously nonstenotic, mostly lipid-rich, 'vulnerable' plaques [133–135]. Thrombus formation and plaque rupture play key roles in the onset of acute coronary syndrome. Plaque rupture is the most frequent cause of acute myocardial infarction and it has been recognized that thin-cap fibroatheroma (TCFA) is the primary plaque type at the site of plaque rupture [136–138]. With the hope of guiding patient management, coronary artery plaque composition has been extensively studied using invasive imaging techniques such as intravascular ultrasound and, more recently, optical coherence tomography [139–141]. However, the complexity, associated costs, invasiveness and restricted availability limit a more extensive clinical application of these modalities beyond specific clinical scenarios and research. To overcome some of these hurdles, CT coronary angiography, with its high temporal and spatial resolution, has been the subject of research to investigate the potential of an attenuation-based plaque detection and characterization. Studies have shown that CT is able to analyze coronary plaques quantitatively and qualitatively, especially by assessing the intraplaque density, and it has been shown that CT results correlate reasonably well with histological findings [142–147]. However, a direct comparison of intravascular ultrasound and multislice CT has revealed a general overestimation on multislice CT for quantitative measurements of all areas and thickness [132,148]. The formation of noncalcified plaque is recognized to be frequently associated with positive vascular remodeling, which is detectable on CT. Noncalcified plaques have CT attenuation values between 7 and 152 Hounsfield units (HU) and can be differentiated from epicardial fat (~-30 HU) and unenhanced blood (~40 HU) [130,144,146]. On the basis of *ex vivo* studies, attenuation ranges for specific plaque components according to their HU have been proposed and MDCT has been cited to be able to identify differences in plaque morphologies between TCFA and non-TCFA [137,149]. However, *in vivo* attenuation measurements of coronary artery plaques are complicated by the small size and irregular shapes of target lesions resulting in substantial volume averaging, by substantial overlap in attenuation values of fibrous and lipid-rich plaques, and perturbing influences of contrast attenuation in the adjacent coronary lumen limiting a reliable differentiation beyond a characterization of calcified from noncalcified plaque components [150]. Because of increasing interest

in non-invasive atherosclerotic plaque characterization, a multitude of software solutions have been developed (Figure 2) allowing automated plaque detection and volumetric quantification of calcified and noncalcified atherosclerotic plaque components. Even though the accuracy and precision of these software applications remains largely unverified, they might have the potential to overcome limitations such as underestimation of mixed and noncalcified plaque volumes and a trend to overestimate calcified plaque volumes [143]. Despite promising results, the CT differentiation of lipid-rich content from fibrous content remains challenging due to considerable overlap in the attenuation values of lipid and fibrous tissues, leaving the identification of the truly 'vulnerable' plaque at risk of rupture a technological challenge and questioning the current clinical application beyond mere research [151].

Innovations in CT technology are promising to further enhance the ability of CT in the quantitative analysis of coronary plaques, but their role for a substantial improvement of coronary atherosclerotic plaque characterization in a clinical setting still needs to be evaluated in further studies [152,153].

### *Myocardial perfusion*

Myocardial perfusion imaging (MPI) has proven to be a valuable methodology for assessing the physiologic significance of a stenosis, allowing both a reliable diagnosis and prognosis in patients with CAD to be made [4,22,154–156]. Pharmacologic-induced coronary vasodilation during the infusion of radionuclide tracers has been shown to be as accurate as exercise stress testing with single-photon emission tomography in diagnosing coronary disease [22]. However, sensitivity and specificity of stress testing has been described to be limited with accuracies ranging from 70 to 86%, typically detecting CAD in later stages when significant coronary stenosis is present [157]. By contrast, the morphological evaluation of coronary arteries with CT coronary angiography and the limited ability for dynamic evaluations of the myocardial contrast medium passage with multislice CT have thus far been proven to be unsatisfactory to assess the physiological significance of coronary artery stenosis. Studies investigating the relationship between stenosis of 50% or more at CT coronary angiography and corresponding myocardial perfusion defects at nuclear imaging demonstrated a relatively weak correlation for detecting reversible myocardial perfusion defects with a sensitivity and specificity ranging between 85–95 and 53–79%, respectively [158–160]. Only increasing cut-off thresholds to degrees of stenosis of 70% or more prompted a significant increase in agreement between CT and nuclear studies [158,160]. On the other hand, a comprehensive assessment of myocardial perfusion from physiologic testing and morphologic evaluation of the coronary arteries by means of image fusion of nuclear imaging and coronary CT angiography has been shown to provide incremental diagnostic value over either technique alone. Nevertheless, obtaining diagnostic information on coronary artery morphology and the corresponding myocardial perfusion using one single modality remains a coveted goal [158–160].

Initial research efforts to perform CT myocardial perfusion imaging date back to the era of electron-beam CT and four-row MDCT, which revealed acute myocardial infarctions as hypoattenuated myocardium in animal models [161,162]. The early

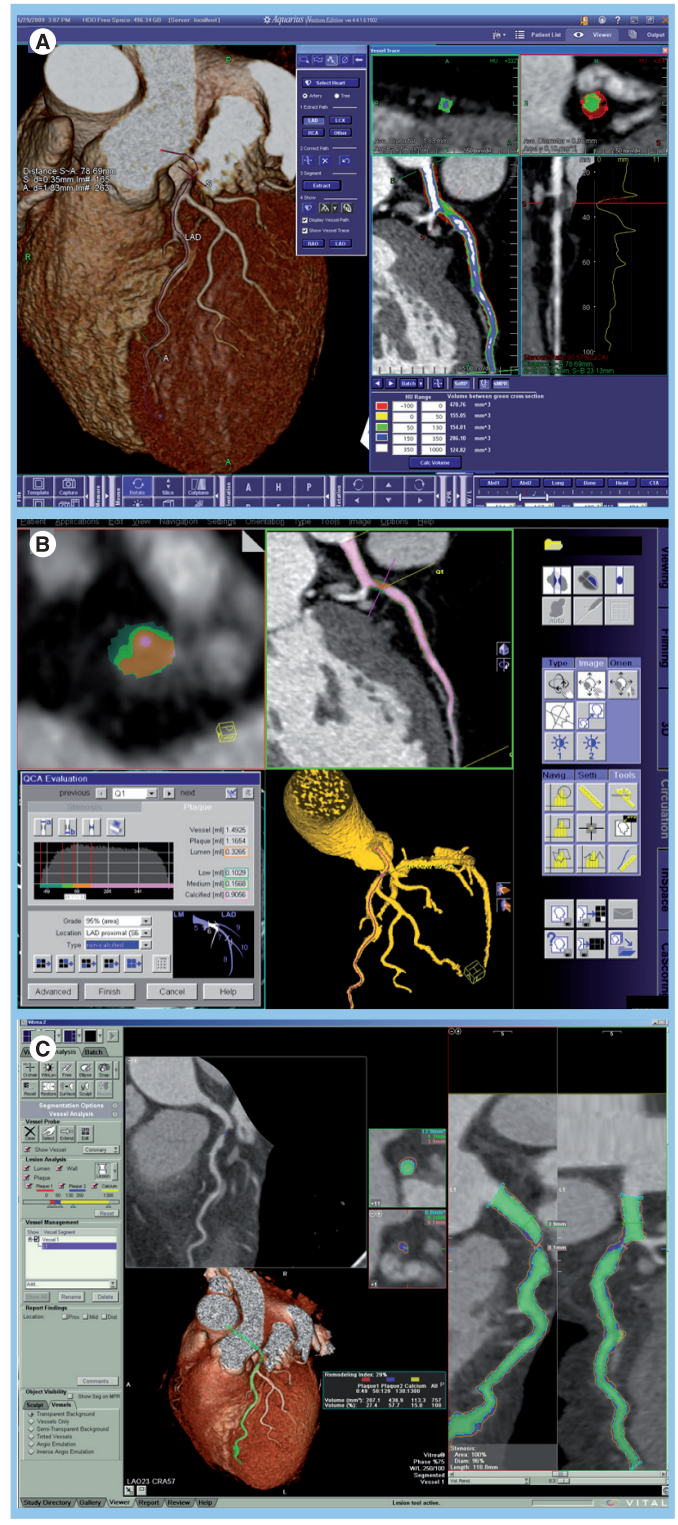


**Figure 2. Overview of different commercially available software solutions allowing dedicated plaque analysis and characterization. (A)** Circulation (Siemens Healthcare, Erlangen, Germany); **(B)** Aquarius (TeraRecon, CA, USA); **(C)** Vitrea (Vital Images, MN, USA).

introduction of these observations into clinical practice showed 91% sensitivity, 79% specificity and 83% accuracy for the CT detection of myocardial infarction [163].

However, only the introduction of the most recent technological advances suggests the feasibility of CT as a standalone modality for an integrative evaluation of all aspects of coronary heart disease [46,47,164–168]. In their study George *et al.* compared the combination of CT coronary angiography and rest–stress CT myocardial perfusion imaging to detect hemodynamically significant stenosis, with the combination of rest–stress single photon emission CT (SPECT) and quantitative coronary angiography as the reference standard using adenosine stress 64- and 256-row CT in 40 patients with abnormal myocardial perfusion SPECT findings [23]. They reported 86%(79%) sensitivity, 92% (91%) specificity, 92% (75%) positive-predictive value and 85% (92%) negative-predictive value on a per-patient (per-vessel territory) analysis, with an estimated mean effective radiation dose of 21.6 mSv for the combined rest and stress 256-row CT imaging and 16.8 mSv for the 64-row stress CT examinations. Initial studies applying DSCT in dual-energy mode have reported good correlation between CT and SPECT studies for detecting decreases in the myocardial blood supply [46,47]. Since dual-energy CT data can be postprocessed in different ways it may have the potential for the detection of obstructive CAD and simultaneously provide information about the hemodynamic consequences of detected lesions on myocardial perfusion from a single dual-energy CT acquisition. Figure 3 provides an example of a perfusion study in a patient presenting with atypical chest pain.

Moreover, second-generation DSCT scanners might be capable of performing dynamic first-pass myocardial CT perfusion (Figure 4). According to initial studies, adenosine-stress dynamic volume CT myocardial perfusion can provide comparable results to MRI for the differentiation between normal and ischemic myocardium, and for the determination of semiquantitative parameters of myocardial blood flow with high specificity and a low rate of false-positive findings [169,170]. In addition, the results of these studies suggest the feasibility of dynamic first-pass perfusion CT to obtain absolute quantitative parameters

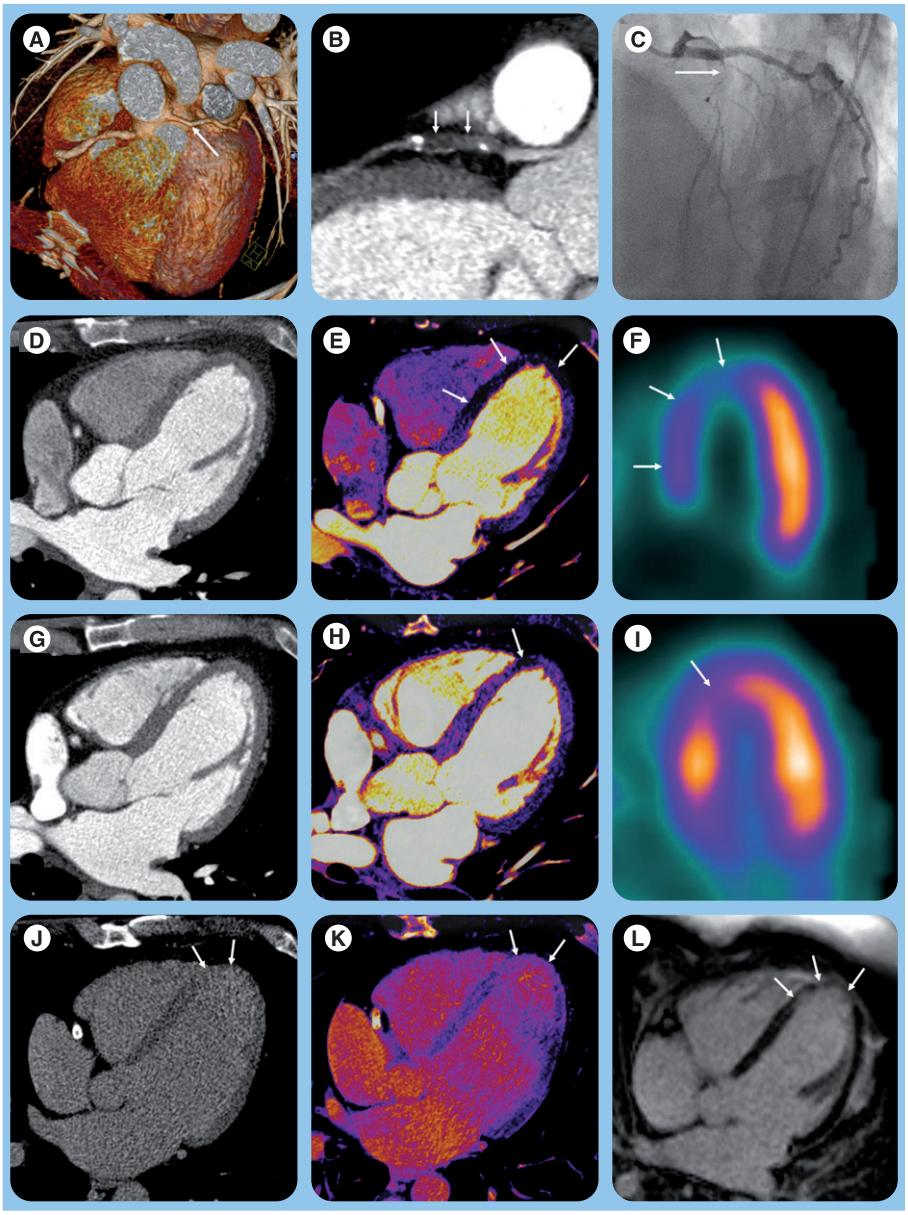


**Figure 3. A 45-year-old man presenting with atypical chest pain. (A)** Volume-rendering technique and **(B)** computed tomography (CT) coronary angiography illustrate a complete occlusion of the proximal left anterior descending artery (LAD; arrows), which was confirmed by **(C)** invasive coronary angiography. **(D)** While the merged gray scale image of myocardial stress-perfusion CT reveals no definite hypo-enhancement of the left ventricular myocardium, **(E)** the four chamber view of adenosine induced stress dual-energy CT (DECT) depicts an extensive perfusion defect (arrows) at ventricular septum and apical portion (arrows) of the left ventricle, which is verified by **(F)** SPECT. **(G)** The merged grayscale image of rest perfusion CT study also shows normal myocardial contrast enhancement. However, rest **(H)** DECT and **(I)** SPECT demonstrate a partially reversible perfusion defect (arrows) in the corresponding LAD territory. **(J)** Delayed enhancement CT identifies subtle delayed hyper-enhancement (arrows) at the left ventricular apex of the left ventricle. The apical iodine uptake is visualized more prominently at the iodine map of **(K)** DECT and confirmed by **(L)** delayed-phase MRI (arrows).

of myocardial blood flow as a moderate correlation between absolute myocardial blood flow quantification and the upslope of the signal intensity over time curve was observed.

Further research efforts are being directed towards optimizing the visualization of perfusion abnormalities. The results of a recent study suggest that minimum-intensity projection and thick multiplanar reformation might be beneficial in the qualitative and quantitative evaluation of infarcted myocardium [171].

### *Myocardial viability*

The identification of dysfunctional but viable myocardium in patients with CAD is of paramount clinical importance since viable myocardium most likely benefits from revascularization, whereas revascularization of scar tissue will not lead to improvement of left ventricular function [172]. Myocardial viability has traditionally been assessed by using nuclear techniques [173,174]. However, the concept of delayed contrast enhancement has been successfully implemented with MRI to identify the location, extent and transmurality of myocardial infarction [175,176]. MRI delayed enhancement imaging reliably detects myocardial scarring and is used clinically to detect occult infarcts, to predict functional recovery after revascularization therapy and to identify risk for future adverse cardiac events, making it the clinical reference standard [177–181].

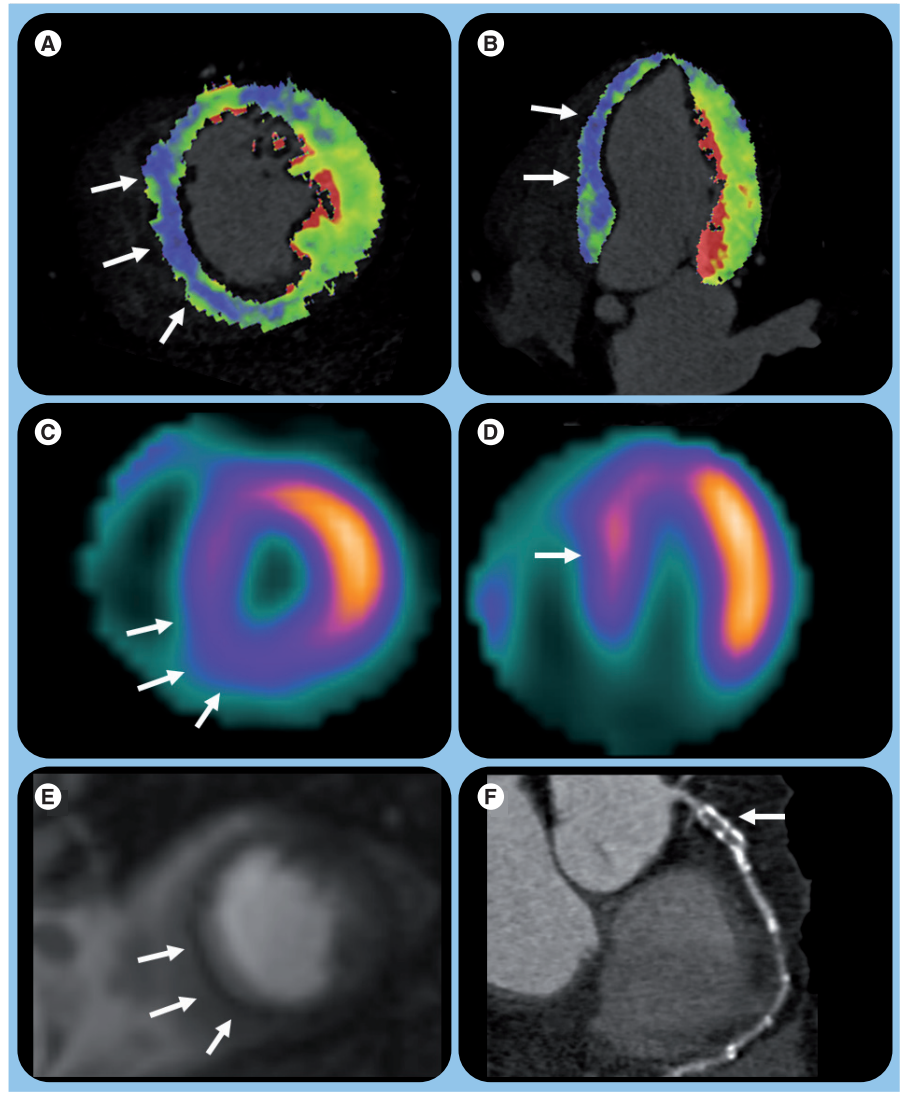


**Figure 4. Dynamic real-time myocardial stress-perfusion in a 50-year-old man presenting with atypical chest pain using second-generation dual-source computed tomography. (A & B)** The absolute quantification of the myocardial perfusion and resulting computed tomography (CT) myocardial blood pool perfusion maps reveal hypo-perfusion (blue color, labeled with arrows) most prominent inferoseptally in the mid-ventricular portion of the left ventricle with decreased myocardial blood flow of approximately 60 ml/100 ml/min. **(C & D)** CT findings were confirmed by SPECT and **(E)** stress-perfusion MRI. **(F)** Curved multiplanar reformat depicting a calcified and noncalcified plaque, causing occlusion of the proximal right coronary artery.

Delayed enhanced imaging using MRI detects accumulations of gadolinium-based contrast material in areas of myocardial necrosis after infarction [175]. In theory, the same principle may apply to cardiac CT since iodine-based intravenous contrast has similar kinetics as gadolinium. It has been repeatedly shown in animal studies that CT can detect iodine accumulation in irreversibly damaged myocardium [182,183]. Furthermore, delayed-enhancement CT has been shown to correlate well with MRI during the different stages of infarction, enabling the assessment of reperfusion during acute, subacute and chronic stages, as well as the accurate degree of transmurality [184–186]. In humans, delayed-enhancement CT and MRI also correlate well; however, CT systematically underestimates the true infarct size compared with MRI [187,188]. To date, no universal agreement on the most suitable protocol for delayed-enhancement CT imaging could be achieved as some studies indicate the highest difference in contrast attenuation between normal and infarcted myocardium occurred 5 min after intravenous contrast injection, whereas intervals of up to 15 min have been proposed by others as well as low-kilovoltage scanning protocols for better contrast differentiation [182,189].

The clinical value of CT viability imaging alone might be limited by the additional amount of radiation, which is approximately 3.8 mSv in female and 2.8 mSv in male patients [190]. However, the integration into a comprehensive scanning protocol might allow a non-invasive patient evaluation using a single modality and has the potential to provide safer and

cheaper assessment with less radiation than the current routine combination of nuclear myocardial perfusion imaging and conventional angiography.

## Conclusion

Computed tomography has been recognized as the most valuable and potentially effective alternative to invasive coronary angiography for the detection and diagnosis of CAD. Owing to its rapid technological development, ongoing refinements and improved diagnostic accuracy, current technical limitations, including the association of coronary CT angiography with relatively high levels of radiation, are increasingly being addressed. The recent introduction of larger detector arrays and two generations of DSCT scanners brought substantial improvements in temporal resolution. New acquisition concepts such as 'high-pitch single-heartbeat acquisitions' have similar potential to reduce radiation dose. It can be expected that improved technology, ongoing development of scan protocols and appropriate clinical studies will further refine the role of cardiac CT in the near future, widening the scope of coronary CT angiography over mere anatomical assessment to a complete analysis of cardiac morphology, function, perfusion and viability. Currently, clinical applications seem most likely in the context of stable and acute chest pain to rule out coronary disease in selected subgroups of individuals who do not have a high pretest likelihood of disease and in whom a negative CT scan would replace an otherwise necessary invasive coronary angiogram.

With appropriate patient selection, it can be expected that cardiac CT can not only accurately diagnose all aspects of heart disease, but also markedly decrease healthcare costs and reliably predict clinical outcomes.

## Expert commentary & five-year view

Computed tomography of the coronary arteries has been performed for more than three decades for the detection of coronary artery calcifications. Moreover, for the last 8 years contrast-enhanced CT coronary angiography has become a clinically accepted methodology for a non-invasive assessment of the coronary arteries achieving an angiographic display. In addition, with rapid innovations and ongoing refinements in technology, current technical limitations, including the association of cardiac CT with relatively high levels of radiation, are being increasingly addressed. Along with an increasing clinical evidence base, the healthcare community is working on appropriateness criteria and defining indication guidelines to guarantee suitable use, curb overutilization and ensure cost–effectiveness. New scanner technologies and innovative applications are constantly being explored and sustain a constant widening of the scope of cardiac CT over mere coronary artery assessment to the complete analysis of cardiac morphology, function, perfusion and viability. Considering all of the above, there is little doubt about the rapidly expanding role and growing importance of cardiac CT as a cornerstone for a comprehensive evaluation of all aspects of CAD.

### Financial & competing interests disclosure

*U Joseph Schoepf is a consultant for and receives research support from Bayer-Schering, Bracco, General Electric, Medrad and Siemens. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.*

*No writing assistance was utilized in the production of this manuscript.*

### Key issues

- To date, the clinically accepted diagnostic value of computed tomography (CT) coronary angiography is focused on a mere morphological evaluation.
- Currently, there is no single modality available to comprehensively evaluate all aspects of coronary artery disease including morphology, function, perfusion and viability.
- Current limitations of cardiac CT include limited temporal resolution, especially in patients with high resting heart rates and irregular heart rhythm, and high levels of radiation exposure.
- Ongoing innovations in scanner technology and acquisition protocols continue to improve the performance and clinical scope of cardiac CT, and enable substantial reductions in radiation exposure.
- Technologies and acquisition protocols are currently being investigated to combine coronary CT angiography with CT-based methods for the evaluation of myocardial function, perfusion and viability to allow a comprehensive assessment of all aspects of coronary artery disease with CT as the sole imaging modality.

## References

Papers of special note have been highlighted as:
• of interest
•• of considerable interest

1 Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: Part II: variations in cardiovascular disease by specific ethnic groups and geographic regions and prevention strategies. *Circulation* 104, 2855–2864 (2001).

2 Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Circulation* 104, 2746–2753 (2001).

3 Quercioli A, Montecucco F, Bertolotto M *et al.* Coronary artery calcification and cardiovascular risk: the role of RANKL/OPG signalling. *Eur. J. Clin. Invest.* 40, 645–654 (2010).

4 Bastarrika G, Lee YS, Huda W, Ruzsics B, Costello P, Schoepf UJ. CT of coronary artery disease. *Radiology* 253, 317–338 (2009).

5 Meijboom WB, Meijs MF, Schuijf JD *et al.* Diagnostic accuracy of 64-slice computed tomography coronary angiography: a prospective, multicenter, multivendor study. *J. Am. Coll. Cardiol.* 52, 2135–2144 (2008).

6 Hadamitzky M, Freissmuth B, Meyer T *et al.* Prognostic value of coronary computed tomographic angiography for prediction of cardiac events in patients with suspected coronary artery disease. *JACC Cardiovasc. Imaging* 2, 404–411 (2009).

7 van der Giessen AG, Toepker MH, Donelly PM *et al.* Reproducibility, accuracy, and predictors of accuracy for the detection of coronary atherosclerotic plaque composition by computed tomography: an *ex vivo* comparison to intravascular ultrasound. *Invest. Radiol.* 45(11), 693–701 (2010).

8 Carrascosa P, Capunay C, Deviggiano A *et al.* Accuracy of low-dose prospectively gated axial coronary CT angiography for the assessment of coronary artery stenosis in patients with stable heart rate. *J. Cardiovasc. Comput. Tomogr.* 4, 197–205 (2010).

9 de Graaf FR, Schuijf JD, van Velzen JE *et al.* Diagnostic accuracy of 320-row multidetector computed tomography coronary angiography to noninvasively assess in-stent restenosis. *Invest. Radiol.* 45, 331–340 (2010).

10 Klepzig H. Diagnostic accuracy of dual-source multi-slice CT-coronary angiography in patients with an intermediate pretest likelihood for coronary artery disease. *Eur. Heart J.* 29, 680 (2008).

11 Leber AW, Johnson T, Becker A *et al.* Diagnostic accuracy of dual-source multi-slice CT-coronary angiography in patients with an intermediate pretest likelihood for coronary artery disease. *Eur. Heart J.* 28, 2354–2360 (2007).

12 Kapoor D, Thompson RC. Diagnostic accuracy of CT coronary angiography. *Cardiol. Clin.* 27, 563–571 (2009).

13 Arnoldi E, Ramos-Duran L, Abro JA *et al.* [Coronary CT angiography using prospective ECG triggering: high diagnostic accuracy with low radiation dose.] *Radiologe* 50, 500–506 (2010).

14 Hessel SJ, Adams DF, Judy PF, Fishbein MC, Abrams HL. Detection of myocardial ischemia *in vitro* by computed tomography. *Radiology* 127, 413–418 (1978).

15 Hilfiker PR, Weishaupt D, Marincek B. Multislice spiral computed tomography of subacute myocardial infarction. *Circulation* 104, 1083 (2001).

16 Juergens KU, Grude M, Fallenberg EM *et al.* Using ECG-gated multidetector CT to evaluate global left ventricular myocardial function in patients with coronary artery disease. *AJR Am. J. Roentgenol.* 179, 1545–1550 (2002).

17 Mahnken AH, Spuntrup E, Wildberger JE *et al.* [Quantification of cardiac function with multislice spiral CT using retrospective EKG-gating: comparison with MRI]. *Rofo* 175, 83–88 (2003).

18 Mochizuki T, Murase K, Higashino H, Koyama Y, Azemoto S, Ikezoe J. Images in cardiovascular medicine. Demonstration of acute myocardial infarction by subsecond spiral computed tomography: early defect and delayed enhancement. *Circulation* 99, 2058–2059 (1999).

19 Mohlenkamp S, Lerman LO, Lerman A *et al.* Minimally invasive evaluation of coronary microvascular function by electron beam computed tomography. *Circulation* 102, 2411–2416 (2000).

20 Willmann JK, Weishaupt D, Lachat M *et al.* Electrocardiographically gated multi-detector row CT for assessment of valvular morphology and calcification in aortic stenosis. *Radiology* 225, 120–128 (2002).

21 Leschka S, Stolzmann P, Desbiolles L *et al.* Diagnostic accuracy of high-pitch dual-source CT for the assessment of coronary stenoses: first experience. *Eur. Radiol.* 19, 2896–2903 (2009).

22 George RT, Silva C, Cordeiro MA *et al.* Multidetector computed tomography myocardial perfusion imaging during adenosine stress. *J. Am. Coll. Cardiol.* 48, 153–160 (2006).

23 George RT, Arbab-Zadeh A, Miller JM *et al.* Adenosine stress 64- and 256-row detector computed tomography angiography and perfusion imaging: a pilot study evaluating the transmural extent of perfusion abnormalities to predict atherosclerosis causing myocardial ischemia. *Circ. Cardiovasc. Imaging* 2, 174–182 (2009).

24 George RT, Jerosch-Herold M, Silva C *et al.* Quantification of myocardial perfusion using dynamic 64-detector computed tomography. *Invest. Radiol.* 42, 815–822 (2007).

25 Shen Y, Qian JY, Wang MH *et al.* Quantitative and qualitative assessment of non-obstructive left main coronary artery plaques using 64-multislice computed tomography compared with intravascular ultrasound. *Chin. Med. J. (Engl.)* 123, 827–833 (2010).

26 van Werkhoven JM, Bax JJ, Nucifora G *et al.* The value of multi-slice-computed tomography coronary angiography for risk stratification. *J. Nucl. Cardiol.* 16, 970–980 (2009).

27 Lipton MJ, Higgins CB, Farmer D, Boyd DP. Cardiac imaging with a high-speed Cine-CT scanner: preliminary results. *Radiology* 152, 579–582 (1984).

28 Achenbach S, Ulzheimer S, Baum U *et al.* Noninvasive coronary angiography by retrospectively ECG-gated multislice spiral CT. *Circulation* 102, 2823–2828 (2000).

29 Kachelriess M, Ulzheimer S, Kalender WA. ECG-correlated image reconstruction from subsecond multi-slice spiral CT scans of the heart. *Med. Phys.* 27, 1881–1902 (2000).

30 Knez A, Becker CR, Leber A *et al.* Usefulness of multislice spiral computed tomography angiography for determination of coronary artery stenoses. *Am. J. Cardiol.* 88, 1191–1194 (2001).

31 Ohnesorge B, Flohr T, Becker C *et al.* Cardiac imaging by means of electrocardiographically gated multisection spiral CT: initial experience. *Radiology* 217, 564–571 (2000).

32 Schroeder S, Kopp AF, Baumbach A *et al.* Noninvasive detection and evaluation of atherosclerotic coronary plaques with multislice computed tomography. *J. Am. Coll. Cardiol.* 37, 1430–1435 (2001).

33 Klingenbeck-Regn K, Schaller S, Flohr T, Ohnesorge B, Kopp AF, Baum U. Subsecond multi-slice computed tomography: basics and applications. *Eur. J. Radiol.* 31, 110–124 (1999).

34 Dewey M, Hoffmann H, Hamm B. CT coronary angiography using 16 and 64 simultaneous detector rows: intraindividual comparison. *Rofo* 179, 581–586 (2007).

35 Hamon M, Morello R, Riddell JW. Coronary arteries: diagnostic performance of 16- versus 64-section spiral CT compared with invasive coronary angiography – meta-analysis. *Radiology* 245, 720–731 (2007).

36 Flohr T, Stierstorfer K, Raupach R, Ulzheimer S, Bruder H. Performance evaluation of a 64-slice CT system with z-flying focal spot. *Rofo* 176, 1803–1810 (2004).

37 Herzog C, Britten M, Balzer JO *et al.* Multidetector-row cardiac CT: diagnostic value of calcium scoring and CT coronary angiography in patients with symptomatic, but atypical, chest pain. *Eur. Radiol.* 14, 169–177 (2004).

38 Leschka S, Wildermuth S, Boehm T *et al.* Noninvasive coronary angiography with 64-section CT: effect of average heart rate and heart rate variability on image quality. *Radiology* 241, 378–385 (2006).

39 Flohr TG, McCollough CH, Bruder H *et al.* First performance evaluation of a dual-source CT (DSCT) system. *Eur. Radiol.* 16, 256–268 (2006).

40 Johnson TR, Nikolaou K, Wintersperger BJ *et al.* Dual-source CT cardiac imaging: initial experience. *Eur. Radiol.* 16, 1409–1415 (2006).

• **Overview about initial experience using dual-source computed tomography (CT) for cardiac imaging.**

41 Achenbach S, Marwan M, Ropers D *et al.* Coronary computed tomography angiography with a consistent dose below 1 mSv using prospectively electrocardiogram-triggered high-pitch spiral acquisition. *Eur. Heart J.* 31, 340–346 (2009).

42 Flohr TG, Leng S, Yu L *et al.* Dual-source spiral CT with pitch up to 3.2 and 75 ms temporal resolution: image reconstruction and assessment of image quality. *Med. Phys.* 36, 5641–5653 (2009).

• **Overview of new imaging approaches using high-pitch concepts.**

43 Mori S, Endo M, Nishizawa K, Murase K, Fujiwara H, Tanada S. Comparison of patient doses in 256-slice CT and 16-slice CT scanners. *Br. J. Radiol.* 79, 56–61 (2006).

44 Rybicki FJ, Otero HJ, Steigner ML *et al.* Initial evaluation of coronary images from 320-detector row computed tomography. *Int. J. Cardiovasc. Imaging* 24, 535–546 (2008).

45 Kido T, Kurata A, Higashino H *et al.* Cardiac imaging using 256-detector row four-dimensional CT: preliminary clinical report. *Radiat. Med.* 25, 38–44 (2007).

46 Ruzsics B, Lee H, Powers ER, Flohr TG, Costello P, Schoepf UJ. Images in cardiovascular medicine. Myocardial ischemia diagnosed by dual-energy computed tomography: correlation with single-photon emission computed tomography. *Circulation* 117, 1244–1245 (2008).

47 Ruzsics B, Lee H, Zwerner PL, Gebregziabher M, Costello P, Schoepf UJ. Dual-energy CT of the heart for diagnosing coronary artery stenosis and myocardial ischemia-initial experience. *Eur. Radiol.* 18, 2414–2424 (2008).

48 Johnson TR, Krauss B, Sedlmair M *et al.* Material differentiation by dual energy CT: initial experience. *Eur. Radiol.* 17, 1510–1517 (2007).

49 Flohr TG, Klotz E, Allmendinger T, Raupach R, Bruder H, Schmidt B. Pushing the envelope: new computed tomography techniques for cardiothoracic imaging. *J. Thorac. Imaging* 25, 100–111 (2010).

•• **Provides an overview of existing and emerging technologies for cardiothoracic imaging.**

50 Thibault JB, Sauer KD, Bouman CA, Hsieh J. A three-dimensional statistical approach to improved image quality for multislice helical CT. *Med. Phys.* 34, 4526–4544 (2007).

51 Greenland P, Bonow RO, Brundage BH *et al.* ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography). *Circulation* 115, 402–426 (2007).

52 Oudkerk M, Stillman AE, Halliburton SS *et al.* Coronary artery calcium screening: current status and recommendations from the European Society of Cardiac Radiology and North American Society for Cardiovascular Imaging. *Eur. Radiol.* 18, 2785–2807 (2008).

53 Rumberger JA. Tomographic plaque imaging with CT: technical considerations and capabilities. *Prog. Cardiovasc. Dis.* 46, 123–134 (2003).

54 Budoff MJ, Achenbach S, Blumenthal RS *et al.* Assessment of coronary artery disease by cardiac computed tomography: a scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. *Circulation* 114, 1761–1791 (2006).

55 Mahabadi AA, Bamberg F, Toepker M *et al.* Association of aortic valve calcification to the presence, extent, and composition of coronary artery plaque burden: from the Rule Out Myocardial Infarction using Computer Assisted Tomography (ROMICAT) trial. *Am. Heart J.* 158, 562–568 (2009).

56 Sun Z, Ng KH. Multislice CT angiography in cardiac imaging. Part II: clinical applications in coronary artery disease. *Singapore Med. J.* 51, 282–289 (2010).

57 Budoff MJ, Shaw LJ, Liu ST *et al.* Long-term prognosis associated with coronary calcification: observations from a registry of 25,253 patients. *J. Am. Coll. Cardiol.* 49, 1860–1870 (2007).

58 Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. *JAMA* 291, 210–215 (2004).

59 Min JK, Lin FY, Gidseg DS *et al.* Determinants of coronary calcium conversion among patients with a normal coronary calcium scan: what is the 'warranty period' for remaining normal? *J. Am. Coll. Cardiol.* 55, 1110–1117 (2010).

60 Raggi P, Gongora MC, Gopal A, Callister TQ, Budoff M, Shaw LJ. Coronary artery calcium to predict all-cause mortality in elderly men and women. *J. Am. Coll. Cardiol.* 52, 17–23 (2008).

61 Rozanski A, Gransar H, Wong ND *et al.* Clinical outcomes after both coronary calcium scanning and exercise myocardial perfusion scintigraphy. *J. Am. Coll. Cardiol.* 49, 1352–1361 (2007).

62 Detrano R, Guerci AD, Carr JJ *et al.* Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N. Engl. J. Med.* 358, 1336–1345 (2008).

63 Cheng VY, Lepor NE, Madyoon H, Eshaghian S, Naraghi AL, Shah PK. Presence and severity of noncalcified coronary plaque on 64-slice computed tomographic coronary angiography in patients with zero and low coronary artery calcium. *Am. J. Cardiol.* 99, 1183–1186 (2007).

64 Henneman MM, Schuijf JD, Pundziute G *et al.* Noninvasive evaluation with multislice computed tomography in suspected acute coronary syndrome: plaque morphology on multislice computed tomography versus coronary calcium score. *J. Am. Coll. Cardiol.* 52, 216–222 (2008).

65 Marwan M, Ropers D, Pflederer T, Daniel WG, Achenbach S. Clinical characteristics of patients with obstructive coronary lesions in the absence of coronary calcification: an evaluation by coronary CT angiography. *Heart* 95, 1056–1060 (2009).

66 Rubinshtein R, Gaspar T, Halon DA, Goldstein J, Peled N, Lewis BS. Prevalence and extent of obstructive coronary artery disease in patients with zero or low calcium score undergoing 64-slice cardiac multidetector computed tomography for evaluation of a chest pain syndrome. *Am. J. Cardiol.* 99, 472–475 (2007).

67 van der Bijl N, de Bruin PW, Geleijns J *et al.* Assessment of coronary artery calcium by using volumetric 320-row multi-detector computed tomography: comparison of 0.5 mm with 3.0 mm slice reconstructions. *Int. J. Cardiovasc. Imaging* 26, 473–482 (2010).

68 Budoff MJ, Gul KM. Expert review on coronary calcium. *Vasc. Health Risk Manag.* 4, 315–324 (2008).

69 Polonsky TS, McClelland RL, Jorgensen NW *et al.* Coronary artery calcium score and risk classification for coronary heart disease prediction. *JAMA* 303, 1610–1616 (2010).

70 Nieman K, Cademartiri F, Lemos PA, Raaijmakers R, Pattynama PM, de Feyter PJ. Reliable noninvasive coronary angiography with fast submillimeter multislice spiral computed tomography. *Circulation* 106, 2051–2054 (2002).

71 Sun Z, Jiang W. Diagnostic value of multislice computed tomography angiography in coronary artery disease: a meta-analysis. *Eur. J. Radiol.* 60, 279–286 (2006).

72 Budoff MJ, Dowe D, Jollis JG *et al.* Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. *J. Am. Coll. Cardiol.* 52, 1724–1732 (2008).

73 Miller JM, Rochitte CE, Dewey M *et al.* Diagnostic performance of coronary angiography by 64-row CT. *N. Engl. J. Med.* 359, 2324–2336 (2008).

74 Fine JJ, Hopkins CB, Ruff N, Newton FC. Comparison of accuracy of 64-slice cardiovascular computed tomography with coronary angiography in patients with suspected coronary artery disease. *Am. J. Cardiol.* 97, 173–174 (2006).

75 Husmann L, Schepis T, Scheffel H *et al.* Comparison of diagnostic accuracy of 64-slice computed tomography coronary angiography in patients with low, intermediate, and high cardiovascular risk. *Acad. Radiol.* 15, 452–461 (2008).

76 Leschka S, Alkadhi H, Plass A *et al.* Accuracy of MSCT coronary angiography with 64-slice technology: first experience. *Eur. Heart J.* 26, 1482–1487 (2005).

77 Ropers U, Ropers D, Pflederer T *et al.* Influence of heart rate on the diagnostic accuracy of dual-source computed tomography coronary angiography. *J. Am. Coll. Cardiol.* 50, 2393–2398 (2007).

78 Min JK, Feignoux J, Treutenaere J, Laperche T, Sablayrolles J. The prognostic value of multidetector coronary CT angiography for the prediction of major adverse cardiovascular events: a multicenter observational cohort study. *Int. J. Cardiovasc. Imaging* 26, 721–728 (2010).

79 Husmann L, Gaemperli O, Schepis T *et al.* Accuracy of quantitative coronary angiography with computed tomography and its dependency on plaque composition: plaque composition and accuracy of cardiac CT. *Int. J. Cardiovasc. Imaging* 24, 895–904 (2008).

80 Raff GL, Gallagher MJ, O'Neill WW, Goldstein JA. Diagnostic accuracy of noninvasive coronary angiography using 64-slice spiral computed tomography. *J. Am. Coll. Cardiol.* 46, 552–557 (2005).

81 Ropers D, Rixe J, Anders K *et al.* Usefulness of multidetector row spiral computed tomography with 64- × 0.6-mm collimation and 330-ms rotation for the noninvasive detection of significant coronary artery stenoses. *Am. J. Cardiol.* 97, 343–348 (2006).

82 Boll DT, Merkle EM, Paulson EK, Fleiter TR. Coronary stent patency: dual-energy multidetector CT assessment in a pilot study with anthropomorphic phantom. *Radiology* 247, 687–695 (2008).

83 Boll DT, Merkle EM, Paulson EK, Mirza RA, Fleiter TR. Calcified vascular plaque specimens: assessment with cardiac dual-energy multidetector CT in anthropomorphically moving heart phantom. *Radiology* 249, 119–126 (2008).

84 Oncel D, Oncel G, Tastan A. Effectiveness of dual-source CT coronary angiography for the evaluation of coronary artery disease in patients with atrial fibrillation: initial experience. *Radiology* 245, 703–711 (2007).

85 Schoepf UJ, Zwerner PL, Savino G, Herzog C, Kerl JM, Costello P. Coronary CT angiography. *Radiology* 244, 48–63 (2007).

86 Arnoldi E, Gebregziabher M, Schoepf UJ *et al.* Automated computer-aided stenosis detection at coronary CT angiography: initial experience. *Eur. Radiol.* 20, 1160–1167 (2010).

87 Hendel RC, Patel MR, Kramer CM *et al.* ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group, American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology. *J. Am. Coll. Cardiol.* 48, 1475–1497 (2006).

•• **Provides guidance for appropriate use of cardiac CT and MRI.**

88 Jacobs JE, Boxt LM, Desjardins B, Fishman EK, Larson PA, Schoepf J. ACR practice guideline for the performance and interpretation of cardiac computed tomography (CT). *J. Am. Coll. Radiol.* 3, 677–685 (2006).

89 Kitagawa K, Choi BW, Chan C *et al.* ASCI 2010 appropriateness criteria for cardiac magnetic resonance imaging: a report of the Asian Society of Cardiovascular Imaging cardiac computed tomography and cardiac magnetic resonance imaging guideline working group. *Int. J. Cardiovasc. Imaging* 26(Suppl. 1), 1–15 (2010).

90 Schoepf UJ, Becker CR, Obuchowski NA *et al.* Multi-slice computed tomography as a screening tool for colon cancer, lung cancer and coronary artery disease. *Eur. Radiol.* 11, 1975–1985 (2001).

91 Schroeder S, Achenbach S, Bengel F *et al.* Cardiac computed tomography: indications, applications, limitations, and training requirements: report of a Writing Group deployed by the Working Group Nuclear Cardiology and Cardiac CT of the European Society of Cardiology and the European Council of Nuclear Cardiology. *Eur. Heart J.* 29, 531–556 (2008).

92 Stillman AE, Oudkerk M, Ackerman M *et al.* Use of multidetector computed tomography for the assessment of acute chest pain: a consensus statement of the North American Society of Cardiac Imaging and the European Society of Cardiac Radiology. *Eur. Radiol.* 17, 2196–2207 (2007).

93 Tsai IC, Choi BW, Chan C *et al.* ASCI 2010 appropriateness criteria for cardiac computed tomography: a report of the Asian Society of Cardiovascular Imaging Cardiac Computed Tomography and Cardiac Magnetic Resonance Imaging Guideline Working Group. *Int. J. Cardiovasc. Imaging* 26(Suppl. 1), 1–15 (2010).

94 Henzler T, Hanley M, Arnoldi E, Bastarrika G, Schoepf UJ, Becker HC. Practical strategies for low radiation dose cardiac computed tomography. *J. Thorac. Imaging* 25, 213–220 (2010).

• **Provides overview about up-to-date dose-reduction strategies.**

95 Chow BJ, Hoffmann U, Nieman K. Computed tomographic coronary angiography: an alternative to invasive coronary angiography. *Can. J. Cardiol.* 21, 933–940 (2005).

96 Haberl R, Tittus J, Bohme E *et al.* Multislice spiral computed tomographic angiography of coronary arteries in patients with suspected coronary artery disease: an effective filter before catheter angiography? *Am. Heart J.* 149, 1112–1119 (2005).

97 Schoepf UJ, Becker CR, Ohnesorge BM, Yucel EK. CT of coronary artery disease. *Radiology* 232, 18–37 (2004).

98 Onuma Y, Tanabe K, Chihara R *et al.* Evaluation of coronary artery bypass grafts and native coronary arteries using 64-slice multidetector computed tomography. *Am. Heart J.* 154, 519–526 (2007).

99 Lee R, Lim J, Kaw G, Wan G, Ng K, Ho KT. Comprehensive noninvasive evaluation of bypass grafts and native coronary arteries in patients after coronary bypass surgery: accuracy of 64-slice multidetector computed tomography compared with invasive coronary angiography. *J. Cardiovasc. Med. (Hagerstown)* 11, 81–90 (2010).

100 Auguadro C, Manfredi M, Scalise F *et al.* Multislice computed tomography for the evaluation of coronary bypass grafts and native coronary arteries: comparison with traditional angiography. *J. Cardiovasc. Med. (Hagerstown)* 10, 454–460 (2009).

101 Feuchtner GM, Schachner T, Bonatti J *et al.* Diagnostic performance of 64-slice computed tomography in evaluation of coronary artery bypass grafts. *AJR Am. J. Roentgenol.* 189, 574–580 (2007).

102 Nikolaou K, Saam T, Rist C *et al.* [Pre- and postsurgical diagnostics with dual-source computed tomography in cardiac surgery]. *Radiologe* 47, 310–318 (2007).

103 Newell MC, Henry CR, Sigakis CJ *et al.* Comparison of safety and efficacy of sirolimus-eluting stents versus bare metal stents in patients with ST-segment elevation myocardial infarction. *Am. J. Cardiol.* 97, 1299–1302 (2006).

104 Funabashi N, Komiyama N, Komuro I. Patency of coronary artery lumen surrounded by metallic stent evaluated by three dimensional volume rendering images using ECG gated multislice computed tomography. *Heart* 89, 388 (2003).

105 Pump H, Mohlenkamp S, Sehnert CA *et al.* Coronary arterial stent patency: assessment with electron-beam CT. *Radiology* 214, 447–452 (2000).

106 Kruger S, Mahnken AH, Sinha AM *et al.* Multislice spiral computed tomography for the detection of coronary stent restenosis and patency. *Int. J. Cardiol.* 89, 167–172 (2003).

107 Maintz D, Grude M, Fallenberg EM, Heindel W, Fischbach R. Assessment of coronary arterial stents by multislice-CT angiography. *Acta Radiol.* 44, 597–603 (2003).

108 Maintz D, Seifarth H, Raupach R *et al.* 64-slice multidetector coronary CT angiography: *in vitro* evaluation of 68 different stents. *Eur. Radiol.* 16, 818–826 (2006).

109 Hamon M, Champ-Rigot L, Morello R, Riddell JW, Hamon M. Diagnostic accuracy of in-stent coronary restenosis detection with multislice spiral computed tomography: a meta-analysis. *Eur. Radiol.* 18, 217–225 (2008).

110 Pugliese F, Weustink AC, Van Mieghem C *et al.* Dual source coronary computed tomography angiography for detecting in-stent restenosis. *Heart* 94, 848–854 (2008).

111 Oncel D, Oncel G, Tastan A, Tamci B. Evaluation of coronary stent patency and in-stent restenosis with dual-source CT coronary angiography without heart rate control. *AJR Am. J. Roentgenol.* 191, 56–63 (2008).

112 Sun Z, Davidson R, Lin CH. Multi-detector row CT angiography in the assessment of coronary in-stent restenosis: a systematic review. *Eur. J. Radiol.* 69, 489–495 (2009).

113 Ghali JK, Liao Y, Simmons B, Castaner A, Cao G, Cooper RS. The prognostic role of left ventricular hypertrophy in patients with or without coronary artery disease. *Ann. Intern. Med.* 117, 831–836 (1992).

114 Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N. Engl. J. Med.* 322, 1561–1566 (1990).

115 Manyari DE. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N. Engl. J. Med.* 323, 1706–1707 (1990).

116 White HD, Norris RM, Brown MA, Brandt PW, Whitlock RM, Wild CJ. Left ventricular end-systolic volume as the major determinant of survival after recovery from myocardial infarction. *Circulation* 76, 44–51 (1987).

117 Busch S, Johnson TR, Wintersperger BJ *et al.* Quantitative assessment of left ventricular function with dual-source CT in comparison to cardiac magnetic resonance imaging: initial findings. *Eur. Radiol.* 18, 570–575 (2008).

118 Gilard M, Pennec PY, Cornily JC *et al.* Multi-slice computer tomography of left ventricular function with automated analysis software in comparison with conventional ventriculography. *Eur. J. Radiol.* 59, 270–275 (2006).

119 van der Vleuten PA, de Jonge GJ, Lubbers DD *et al.* Evaluation of global left ventricular function assessment by dual-source computed tomography compared with MRI. *Eur. Radiol.* 19, 271–277 (2009).

120 Juergens KU, Grude M, Maintz D *et al.* Multi-detector row CT of left ventricular function with dedicated analysis software versus MR imaging: initial experience. *Radiology* 230, 403–410 (2004).

121 Dirksen MS, Bax JJ, de Roos A *et al.* Usefulness of dynamic multislice computed tomography of left ventricular function in unstable angina pectoris and comparison with echocardiography. *Am. J. Cardiol.* 90, 1157–1160 (2002).

122 Fischbach R, Juergens KU, Ozgun M *et al.* Assessment of regional left ventricular function with multidetector-row computed tomography versus magnetic resonance imaging. *Eur. Radiol.* 17, 1009–1017 (2007).

123 Halliburton SS, Petersilka M, Schvartzman PR, Obuchowski N, White RD. Evaluation of left ventricular dysfunction using multiphasic reconstructions of coronary multi-slice computed tomography data in patients with chronic ischemic heart disease: validation against cine magnetic resonance imaging. *Int. J. Cardiovasc. Imaging* 19, 73–83 (2003).

124 Henneman MM, Schuijf JD, Jukema JW *et al.* Assessment of global and regional left ventricular function and volumes with 64-slice MSCT: a comparison with 2D echocardiography. *J. Nucl. Cardiol.* 13, 480–487 (2006).

125 Mahnken AH, Koos R, Katoh M *et al.* Sixteen-slice spiral CT versus MR imaging for the assessment of left ventricular function in acute myocardial infarction. *Eur. Radiol.* 15, 714–720 (2005).

126 Pflederer T, Ho KT, Anger T *et al.* Assessment of regional left ventricular function by dual source computed tomography: interobserver variability and validation to laevocardiography. *Eur. J. Radiol.* 72, 85–91 (2009).

127 Bastarrika G, Arraiza M, De Cecco CN, Mastrobuoni S, Ubilla M, Rabago G. Quantification of left ventricular function and mass in heart transplant recipients using dual-source CT and MRI: initial clinical experience. *Eur. Radiol.* 18, 1784–1790 (2008).

128 Bastarrika G, Arraiza M, De Cecco CN *et al.* Dual-source CT in heart transplant recipients: quantification of global left ventricular function and mass. *J. Thorac. Imaging* 24, 103–109 (2009).

129 Mahnken AH, Muhlenbruch G, Koos R *et al.* Automated vs. manual assessment of left ventricular function in cardiac multidetector row computed tomography: comparison with magnetic resonance imaging. *Eur. Radiol.* 16, 1416–1423 (2006).

130 Achenbach S, Moselewski F, Ropers D *et al.* Detection of calcified and noncalcified coronary atherosclerotic plaque by contrast-enhanced, submillimeter multidetector spiral computed tomography: a segment-based comparison with intravascular ultrasound. *Circulation* 109, 14–17 (2004).

131 Becker CR, Knez A, Ohnesorge B, Schoepf UJ, Reiser MF. Imaging of noncalcified coronary plaques using helical CT with retrospective ECG gating. *AJR Am. J. Roentgenol.* 175, 423–424 (2000).

132 Leber AW, Knez A, von Ziegler F *et al.* Quantification of obstructive and nonobstructive coronary lesions by 64-slice computed tomography: a comparative study with quantitative coronary angiography and intravascular ultrasound. *J. Am. Coll. Cardiol.* 46, 147–154 (2005).

133 Burke AP, Farb A, Malcom GT, Liang YH, Smialek J, Virmani R. Coronary risk factors and plaque morphology in men with coronary disease who died suddenly. *N. Engl. J. Med.* 336, 1276–1282 (1997).

134 Leber AW, Knez A, White CW *et al.* Composition of coronary atherosclerotic plaques in patients with acute myocardial infarction and stable angina pectoris determined by contrast-enhanced multislice computed tomography. *Am. J. Cardiol.* 91, 714–718 (2003).

135 Libby P. Molecular bases of the acute coronary syndromes. *Circulation* 91, 2844–2850 (1995).

136 Cheruvu PK, Finn AV, Gardner C *et al.* Frequency and distribution of thin-cap fibroatheroma and ruptured plaques in human coronary arteries: a pathologic study. *J. Am. Coll. Cardiol.* 50, 940–949 (2007).

137 Kashiwagi M, Tanaka A, Kitabata H *et al.* Feasibility of noninvasive assessment of thin-cap fibroatheroma by multidetector computed tomography. *JACC Cardiovasc. Imaging* 2, 1412–1419 (2009).

138 Kashiwagi M, Tanaka A, Kitabata H *et al.* Relationship between coronary arterial remodeling, fibrous cap thickness and high-sensitivity C-reactive protein levels in patients with acute coronary syndrome. *Circ. J.* 73, 1291–1295 (2009).

139 Nissen SE, Yock P. Intravascular ultrasound: novel pathophysiological insights and current clinical applications. *Circulation* 103, 604–616 (2001).

140 Yabushita H, Bouma BE, Houser SL *et al.* Characterization of human atherosclerosis by optical coherence tomography. *Circulation* 106, 1640–1645 (2002).

141 Fujii K, Kawasaki D, Masutani M *et al.* OCT assessment of thin-cap fibroatheroma distribution in native coronary arteries. *JACC Cardiovasc. Imaging* 3, 168–175 (2010).

142 Achenbach S, Ropers D, Hoffmann U *et al.* Assessment of coronary remodeling in stenotic and nonstenotic coronary atherosclerotic lesions by multidetector spiral computed tomography. *J. Am. Coll. Cardiol.* 43, 842–847 (2004).

143 Leber AW, Becker A, Knez A *et al.* Accuracy of 64-slice computed tomography to classify and quantify plaque volumes in the proximal coronary system: a comparative study using intravascular ultrasound. *J. Am. Coll. Cardiol.* 47, 672–677 (2006).

144 Sun J, Zhang Z, Lu B *et al.* Identification and quantification of coronary atherosclerotic plaques: a comparison of 64-MDCT and intravascular ultrasound. *AJR Am. J. Roentgenol.* 190, 748–754 (2008).

145 Becker CR, Nikolaou K, Muders M *et al.* *Ex vivo* coronary atherosclerotic plaque characterization with multi-detector-row CT. *Eur. Radiol.* 13, 2094–2098 (2003).

146 Leber AW, Knez A, Becker A *et al.* Accuracy of multidetector spiral computed tomography in identifying and differentiating the composition of coronary atherosclerotic plaques: a comparative study with intracoronary ultrasound. *J. Am. Coll. Cardiol.* 43, 1241–1247 (2004).

147 Moselewski F, Ropers D, Pohle K *et al.* Comparison of measurement of cross-sectional coronary atherosclerotic plaque and vessel areas by 16-slice multidetector computed tomography versus intravascular ultrasound. *Am. J. Cardiol.* 94, 1294–1297 (2004).

148 Chopard R, Boussel L, Motreff P *et al.* How reliable are 40 MHz IVUS and 64-slice MDCT in characterizing coronary plaque composition? An *ex vivo* study with histopathological comparison. *Int. J. Cardiovasc. Imaging* 26, 373–383 (2010).

149 Galonska M, Ducke F, Kertesz-Zborilova T, Meyer R, Guski H, Knollmann FD. Characterization of atherosclerotic plaques in human coronary arteries with 16-slice multidetector row computed tomography by analysis of attenuation profiles. *Acad. Radiol.* 15, 222–230 (2008).

150 Schroeder S, Kuettner A, Leitritz M *et al.* Reliability of differentiating human coronary plaque morphology using contrast-enhanced multislice spiral computed tomography: a comparison with histology. *J. Comput. Assist. Tomogr.* 28, 449–454 (2004).

151 Matter CM, Stuber M, Nahrendorf M. Imaging of the unstable plaque: how far have we got? *Eur. Heart J.* 30, 2566–2574 (2009).

152 Chao SP, Law WY, Kuo CJ *et al.* The diagnostic accuracy of 256-row computed tomographic angiography compared with invasive coronary angiography in patients with suspected coronary artery disease. *Eur. Heart J.* DOI: 10.1093/eurheartj/ehq072 (2010) (Epub ahead of print).

153 Korosoglou G, Mueller D, Lehrke S *et al.* Quantitative assessment of stenosis severity and atherosclerotic plaque composition using 256-slice computed tomography. *Eur. Radiol.* 20, 1841–1850 (2010).

154 Gupta NC, Esterbrooks DJ, Hilleman DE, Mohiuddin SM. Comparison of adenosine and exercise thallium-201 single-photon emission computed tomography (SPECT) myocardial perfusion imaging. The GE SPECT Multicenter Adenosine Study Group. *J. Am. Coll. Cardiol.* 19, 248–257 (1992).

155 Miller DD, Verani MS. Current status of myocardial perfusion imaging after percutaneous transluminal coronary angioplasty. *J. Am. Coll. Cardiol.* 24, 260–266 (1994).

156 Nguyen T, Heo J, Ogilby JD, Iskandrian AS. Single photon emission computed tomography with thallium-201 during adenosine-induced coronary hyperemia: correlation with coronary arteriography, exercise thallium imaging and two-dimensional echocardiography. *J. Am. Coll. Cardiol.* 16, 1375–1383 (1990).

157 San Roman JA, Vilacosta I, Castillo JA *et al.* Selection of the optimal stress test for the diagnosis of coronary artery disease. *Heart* 80, 370–376 (1998).

158 Gaemperli O, Schepis T, Valenta I *et al.* Functionally relevant coronary artery disease: comparison of 64-section CT angiography with myocardial perfusion SPECT. *Radiology* 248, 414–423 (2008).

159 Hacker M, Jakobs T, Hack N *et al.* Sixty-four slice spiral CT angiography does not predict the functional relevance of coronary artery stenoses in patients with stable angina. *Eur. J. Nucl. Med. Mol. Imaging* 34, 4–10 (2007).

160 Nicol ED, Stirrup J, Reyes E *et al.* Sixty-four-slice computed tomography coronary angiography compared with myocardial perfusion scintigraphy for the diagnosis of functionally significant coronary stenoses in patients with a low to intermediate likelihood of coronary artery disease. *J. Nucl. Cardiol.* 15, 311–318 (2008).

161 Mahnken AH, Bruners P, Katoh M, Wildberger JE, Gunther RW, Buecker A. Dynamic multi-section CT imaging in acute myocardial infarction: preliminary animal experience. *Eur. Radiol.* 16, 746–752 (2006).

162 Wolfkiel CJ, Ferguson JL, Chomka EV *et al.* Measurement of myocardial blood flow by ultrafast computed tomography. *Circulation* 76, 1262–1273 (1987).

163 Nikolaou K, Sanz J, Poon M *et al.* Assessment of myocardial perfusion and viability from routine contrast-enhanced 16-detector-row computed tomography of the heart: preliminary results. *Eur. Radiol.* 15, 864–871 (2005).

164 Choi SI, George RT, Schuleri KH, Chun EJ, Lima JA, Lardo AC. Recent developments in wide-detector cardiac computed tomography. *Int. J. Cardiovasc. Imaging* 25(Suppl. 1), 23–29 (2009).

165 Ruzsics B, Chiaramida SA, Schoepf UJ. Images in cardiology: dual-energy computed tomography imaging of myocardial infarction. *Heart* 95, 180 (2009).

166 Ruzsics B, Schwarz F, Schoepf UJ *et al.* Comparison of dual-energy computed tomography of the heart with single photon emission computed tomography for assessment of coronary artery stenosis and of the myocardial blood supply. *Am. J. Cardiol.* 104, 318–326 (2009).

167 Schwarz F, Ruzsics B, Schoepf UJ *et al.* Dual-energy CT of the heart – principles and protocols. *Eur. J. Radiol.* 68, 423–433 (2008).

- **Overview of dual-energy CT, detailing specific applications and protocols.**

168 Thilo C, Schoepf UJ, Gordon L, Chiaramida S, Serguson J, Costello P. Integrated assessment of coronary anatomy and myocardial perfusion using a retractable SPECT camera combined with 64-slice CT: initial experience. *Eur. Radiol.* 19, 845–856 (2009).

169 Bastarrika G, Ramos-Duran L, Rosenblum MA, Kang DK, Rowe GW, Schoepf UJ. Adenosine-stress dynamic myocardial CT perfusion imaging: initial clinical experience. *Invest. Radiol.* 45, 306–313 (2010).

170 Bastarrika G, Ramos-Duran L, Schoepf UJ *et al.* Adenosine-stress dynamic myocardial volume perfusion imaging with second generation dual-source computed tomography: concepts and first experiences. *J. Cardiovasc. Comput. Tomogr.* 4, 127–135 (2010).

- **Introduction of a novel imaging approach for myocardial perfusion imaging.**

171 Rogers IS, Cury RC, Blankstein R *et al.* Comparison of postprocessing techniques for the detection of perfusion defects by cardiac computed tomography in patients presenting with acute ST-segment elevation myocardial infarction. *J. Cardiovasc. Comput. Tomogr.* 4, 258–266 (2010).

172 Baer FM, Theissen P, Schneider CA *et al.* MRI assessment of myocardial viability: comparison with other imaging techniques. *Rays* 24, 96–108 (1999).

173 Knuuti J, Schelbert HR, Bax JJ. The need for standardisation of cardiac FDG PET imaging in the evaluation of myocardial viability in patients with chronic ischaemic left ventricular dysfunction. *Eur. J. Nucl. Med. Mol. Imaging* 29, 1257–1266 (2002).

174 Wijns W, Vatner SF, Camici PG. Hibernating myocardium. *N. Engl. J. Med.* 339, 173–181 (1998).

175 Kim RJ, Fieno DS, Parrish TB *et al.* Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. *Circulation* 100, 1992–2002 (1999).

176 Lin D, Kramer CM. Late gadolinium-enhanced cardiac magnetic resonance. *Curr. Cardiol. Rep.* 10, 72–78 (2008).

177 Kim RJ, Wu E, Rafael A *et al.* The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. *N. Engl. J. Med.* 343, 1445–1453 (2000).

178 Kwong RY, Chan AK, Brown KA *et al.* Impact of unrecognized myocardial scar detected by cardiac magnetic resonance imaging on event-free survival in patients presenting with signs or symptoms of coronary artery disease. *Circulation* 113, 2733–2743 (2006).

179 Yan AT, Shayne AJ, Brown KA *et al.* Characterization of the peri-infarct zone by contrast-enhanced cardiac magnetic resonance imaging is a powerful predictor of post-myocardial infarction mortality. *Circulation* 114, 32–39 (2006).

180 Klein C, Nekolla SG, Bengel FM *et al.* Assessment of myocardial viability with contrast-enhanced magnetic resonance imaging: comparison with positron emission tomography. *Circulation* 105, 162–167 (2002).

181 Pennell DJ, Sechtem UP, Higgins CB *et al.* Clinical indications for cardiovascular magnetic resonance (CMR): Consensus Panel report. *J. Cardiovasc. Magn. Reson.* 6, 727–765 (2004).

182 Gerber BL, Belge B, Legros GJ *et al.* Characterization of acute and chronic myocardial infarcts by multidetector computed tomography: comparison with contrast-enhanced magnetic resonance. *Circulation* 113, 823–833 (2006).

183 Lardo AC, Cordeiro MA, Silva C *et al.* Contrast-enhanced multidetector computed tomography viability imaging after myocardial infarction: characterization of myocyte death, microvascular obstruction, and chronic scar. *Circulation* 113, 394–404 (2006).

184 Baks T, Cademartiri F, Moelker AD *et al.* Multislice computed tomography and magnetic resonance imaging for the assessment of reperfused acute myocardial infarction. *J. Am. Coll. Cardiol.* 48, 144–152 (2006).

185 Brodoefel H, Klumpp B, Reimann A *et al.* Sixty-four-MSCT in the characterization of porcine acute and subacute myocardial infarction: determination of transmurality in comparison to magnetic resonance imaging and histopathology. *Eur. J. Radiol.* 62, 235–246 (2007).

186 Mahnken AH, Bruners P, Kinzel S *et al.* Late-phase MSCT in the different stages of myocardial infarction: animal experiments. *Eur. Radiol.* 17, 2310–2317 (2007).

187 Nieman K, Shapiro MD, Ferencik M *et al.* Reperfused myocardial infarction: contrast-enhanced 64-section CT in comparison to MR imaging. *Radiology* 247, 49–56 (2008).

188 Sanz J, Weeks D, Nikolaou K *et al.* Detection of healed myocardial infarction with multidetector-row computed tomography and comparison with cardiac magnetic resonance delayed hyperenhancement. *Am. J. Cardiol.* 98, 149–155 (2006).

189 Sigal-Cinqualbre AB, Hennequin R, Abada HT, Chen X, Paul JF. Low-kilovoltage multi-detector row chest CT in adults: feasibility and effect on image quality and iodine dose. *Radiology* 231, 169–174 (2004).

190 Mahnken AH, Koos R, Katoh M *et al.* Assessment of myocardial viability in reperfused acute myocardial infarction using 16-slice computed tomography in comparison to magnetic resonance imaging. *J. Am. Coll. Cardiol.* 45, 2042–2047 (2005).

191 Kuettner A, Beck T, Drosch T *et al.* Image quality and diagnostic accuracy of non-invasive coronary imaging with 16 detector slice spiral computed tomography with 188 ms temporal resolution. *Heart* 91, 938–941 (2005).

192 Mollet NR, Cademartiri F, Krestin GP *et al.* Improved diagnostic accuracy with 16-row multi-slice computed tomography coronary angiography. *J. Am. Coll. Cardiol.* 45, 128–132 (2005).

193 Hoffmann MH, Shi H, Schmitz BL *et al.* Noninvasive coronary angiography with multislice computed tomography. *JAMA* 293, 2471–2478 (2005).

194 Achenbach S, Ropers D, Pohle FK *et al.* Detection of coronary artery stenoses using multi-detector CT with 16 × 0.75 collimation and 375 ms rotation. *Eur. Heart J.* 26, 1978–1986 (2005).

195 Nikolaou K, Knez A, Rist C *et al.* Accuracy of 64-MDCT in the diagnosis of ischemic heart disease. *AJR Am. J. Roentgenol.* 187, 111–117 (2006).

196 Chao SP, Law WY, Kuo CJ *et al.* The diagnostic accuracy of 256-row computed tomographic angiography compared with invasive coronary angiography in patients with suspected coronary artery disease. *Eur. Heart J.* 31, 1916–1923 (2010).

197 Dewey M, Zimmermann E, Deissenrieder F *et al.* Noninvasive coronary angiography by 320-row computed tomography with lower radiation exposure and maintained diagnostic accuracy: comparison of results with cardiac catheterization in a head-to-head pilot investigation. *Circulation* 120, 867–875 (2009).

198 de Graaf FR, Schuijf JD, van Velzen JE *et al.* Diagnostic accuracy of 320-row multidetector computed tomography coronary angiography in the non-invasive evaluation of significant coronary artery disease. *Eur. Heart J.* 31, 1908–1915 (2010).

199 Johnson TR, Nikolaou K, Busch S *et al.* Diagnostic accuracy of dual-source computed tomography in the diagnosis of coronary artery disease. *Invest. Radiol.* 42, 684–691 (2007).

200 Brodoefel H, Burgstahler C, Tsiflikas I *et al.* Dual-source CT: effect of heart rate, heart rate variability, and calcification on image quality and diagnostic accuracy. *Radiology* 247, 346–355 (2008).